ArmaGen's Position on Offering Compassionate Use to Investigational Medicines

As of October 2014

ArmaGen is focused on developing revolutionary therapies for severe neurological disorders. The company is advancing innovative therapies for the treatment of currently unaddressed neurological complications of lysosomal storage disorders (LSDs), as well as neurodegenerative diseases such as Alzheimer's and Parkinson's. We conduct clinical trials independently and in collaboration with industry partners to assess the safety and efficacy of investigational medicines, which if proven, will allow us to obtain the necessary approvals from regulatory authorities to provide patients with broad access to these medicines.

In general, ArmaGen believes that participating in clinical trials is the best way for patients to access medicines prior to approval. In some extreme circumstances when this is not possible, patients with life-threatening diseases or conditions may seek special access to investigational medicines outside of a clinical trial setting. These situations are typically referred to as compassionate use, but can also be known as expanded access, early access, pre-approval access and emergency use.

The clinical development process (which is the process by which a drug is developed and tested for safety and efficacy, and if proven, submitted to regulatory authorities for approval for use) involves controlled testing in humans to ensure both safety and efficacy. Because it is not known during clinical development and prior to regulatory authorization whether an investigational medicine is safe or effective, compassionate use may present numerous risks for the patient and for the clinical development program. For patients, compassionate use may bring potential safety risks or a false sense that the medicine will provide benefit; for the clinical development program, it can delay or jeopardize the approval of a new medicine sought by many.

Conducting clinical trials is extremely complex and challenging. The ultimate goal is the rigorous, controlled testing of the clinical product with the aim of securing regulatory approval and enabling the medicine to be available to as many patients as possible as quickly as possible. ArmaGen has ethical responsibilities to ensure the safety and the quality and integrity of clinical trials to current research participants and future patients. These ethical responsibilities require that strict criteria are applied for compassionate use of our investigational medicines.

ArmaGen considers many factors when deliberating over a request for compassionate use of an investigational medicine, such as the strength of the clinical data, the benefit-risk profile, the impact on the clinical development program, the phase of development, and probability and timing of regulatory approval.

At ArmaGen, a compassionate use program, or a single request for compassionate use of an investigational medicine, can only be considered if **all** of the following conditions are met:

1. The disease or condition being studied is life-threatening.
2. There are no adequate alternative therapies or clinical trials available.
3. Sufficient preliminary efficacy and safety data exist for the drug and/or drug delivery device in order for ArmaGen to make a benefit-risk analysis consistent with the

establishment of a compassionate use program. This would not occur earlier than the end of Phase 2b studies, and depending on the clinical program, potentially even later.
4. Sufficient clinical data is available to identify an appropriate dose.
5. A patient's treating physician and ArmaGen's Vice President of Clinical Affairs both believe there is the potential for the specific patient under consideration to reasonably expect benefit from the treatment, and there is robust evidence to support the possibility that the patient will benefit.
6. Adequate drug supply can be assured to support both the ongoing clinical trials and approved compassionate use, until and if product becomes commercially available.
7. The patient is not eligible or a candidate for one of the ArmaGen-sponsored studies on the therapy. Geographic limitations to participation in a trial would typically not mean a patient is not eligible.
8. Compassionate access will not adversely impact the clinical development program, in particular, the conduct of a pivotal clinical trial that is required for regulatory approval.
9. The request must be made by the patient's treating physician, unsolicited by ArmaGen or any other individual or organization. This request will provide evidence that the patient will have continual access to the level of medical supervision appropriate to safeguard the patient while being exposed to an experimental therapy.

The above criteria are those that ArmaGen will consider in determining whether to offer compassionate use; however, ArmaGen cannot make a guarantee that a compassionate use program will be available, and, even if a compassionate use program is offered, ArmaGen cannot make a guarantee that the investigational medicine will be available to a particular patient.

If all these conditions are met, ArmaGen will consider compassionate use requests from treating physicians subject to local/national laws and regulations. All requests will be evaluated in a fair, unbiased manner.

Patients with exceptional safety risks that have not been sufficiently studied would be excluded. Any pre-approval access to investigational product must always comply with the applicable country-specific laws and regulations, including medicine importation requirements, and approvals from applicable regulatory bodies and by an Institutional Review Board or Ethics Committee from the treating hospital must be secured. If approved, the patient (or his or her guardian) must provide informed consent and consent to comply with the safety and monitoring requirements defined by ArmaGen. The treating physician must also agree to comply with the safety and monitoring requirements. Compassionate use will cease to be made available if, as a result of clinical trials, the product does not demonstrate a positive risk benefit to patients.
For patients that meet ArmaGen's criteria, treating physicians can make a request via compassionateuse@ArmaGen.com.